Survival of syngeneic and allogeneic iPSC-derived neural precursors after spinal grafting in minipigs.

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Public Summary:
In this work, we showed that syngeneic neural progenitor cells, derived from reprogrammed skin fibroblasts could survive and form neurons and glia in the spinal cord of a mini-pig model in the absence of immunosuppression.

Scientific Abstract:
The use of autologous (or syngeneic) cells derived from induced pluripotent stem cells (iPSCs) holds great promise for future clinical use in a wide range of diseases and injuries. It is expected that cell replacement therapies using autologous cells would forego the need for immunosuppression, otherwise required in allogeneic transplantations. However, recent studies have shown the unexpected immune rejection of undifferentiated autologous mouse iPSCs after transplantation. Whether similar immunogenic properties are maintained in iPSC-derived lineage-committed cells (such as neural precursors) is relatively unknown. We demonstrate that syngeneic porcine iPSC-derived neural precursor cell (NPC) transplantation to the spinal cord in the absence of immunosuppression is associated with long-term survival and neuronal and glial differentiation. No tumor formation was noted. Similar cell engraftment and differentiation were shown in spinally injured transiently immunosuppressed swine leukocyte antigen (SLA)-mismatched allogeneic pigs. These data demonstrate that iPSC-NPCs can be grafted into syngeneic recipients in the absence of immunosuppression and that temporary immunosuppression is sufficient to induce long-term immune tolerance after NPC engraftment into spinally injured allogeneic recipients. Collectively, our results show that iPSC-NPCs represent an alternative source of transplantable NPCs for the treatment of a variety of disorders affecting the spinal cord, including trauma, ischemia, or amyotrophic lateral sclerosis.